II. REMARKS/ARGUMENTS

A. Regarding the Amendments

Claims 42-48 are pending. Claims 1-22 have been withdrawn while claims 23-41 have been canceled without prejudice. Applicant respectfully reserves the right to pursue claims 1-41 in the future.

Claims 42-48 have been added. Support for these claims can be found, *inter alia,* in claims 23 to 41 as they were originally submitted and at pages 8, 9, 10, and 11 in the specification. No new matter is added by the amendments. Entering of the amendments is respectfully requested.

B. Regarding the Interview

Applicant's representative wishes to thank the Examiner and her supervisor for the interview granted on February 10, 2005. During the interview, we had a very productive discussion with respect to the invention and how it distinguishes itself from the prior art disclosure. In particular, we discussed that the prior art discloses indolocarbazole derivatives as cytotoxic agents and does not disclose using indolocarbazole derivatives at a non-cytotoxic level, *e.g.,* it does not disclose the use of indolocarbazole derivatives at a non-cytotoxic level as radiosensitizing agents.

C. Rejection under 35 U.S.C. §112, first paragraph

Claims 23-25, 27-30, 32, 33, 35, 38, and 40-41 are rejected as the full scope of the claims are allegedly not enabled. Applicant respectfully submits that claims 23-25, 27-30, 32, 33, 35 and 38 are canceled, thus the rejection is moot. In addition, applicant respectfully submits that this rejection is not applicable to the newly added claims. Therefore, withdrawal of the rejection is respectfully requested.

D. Rejections under 35 U.S.C. §103(a)

Claims 23-25, 27-30, 32, 33, 35, 36 and 38-41 are rejected as allegedly being obvious over Chen et al. (1997) in view of Prudhomme (2000). This rejection is respectfully traversed.

The Office Action suggests that even though one skilled in the art would not have known the radiosensitization effect of certain indolocarbazole derivatives, he or she would still have used indolocarbazole derivatives in combination with radiation therapy to treat cancer or tumor since it was known prior to the present invention that indolocarbazole derivatives are anti-tumor agents. Applicant respectfully points out that the issue is not whether one skilled in the art would have used certain indolocarbazole derivatives as anti-tumor agents in combination with radiation therapy. The present invention is not directed to using indolocarbazole derivatives at a cytotoxic level as anti-tumor agents. The present invention is based on the applicant's discovery that, in addition to their cytotoxicity, indolocarbazole derivatives have radiosensitizing activity at a non-cytotoxic level. In other words, the present invention is directed to a novel use of indolocarbazole derivatives that is associated with using them at a non-cytotoxic level to enhance the radiosensitivity of cells. Therefore, knowing indolocarbazole derivatives as anti-tumor agents at cytotoxic level would not have led one skilled in the art to use indolocarbazole derivatives at non-cytotoxic level as radiosensitizing agents.

In particular, Prudhomme discloses that certain indolocarbazole derivatives have strong cytotoxicity and such cytotoxicity corresponds to their inhibitory effect on tumor growth. Prudhomme also uses cytotoxicity as a measurement or direct indication of the anti-tumor effect of indolocarbazole derivatives. For example, Prudhomme states that "NB-506 inhibited the growth of various tumor cell lines...and its cytotoxicity was found to be cell line selective." (page 1193, beginning of the second paragraph in the left column). See also the paragraph bridging page 1197 and 1198, page 1198, last paragraph in the left column, and page 1203 and Table 10.

In contrast, the present invention teaches the use of indolocarbazole derivatives that is not based on their cytotoxic effect, but their radiosensitizing activity at non-cytotoxic level. As demonstrated in Example 2, indolocarbazole derivatives of the present invention are potent inducers at non-cytotoxic concentrations. Specifically, unlike camptothecin which requires cytotoxic concentrations for its radiosensitizing activity, the indolocarbazole derivatives of the present invention, *e.g.,* F1, F5, and F7, induced radiosensitization in human MCF-7 and Chinese hamster CHO cells at non-cytotoxic concentrations of 2 μg/ml and 10 μg/ml.

In summary, the present invention is directed to a novel use of indolocarbazole derivatives associated with using them at a non-cytotoxic level. Neither Chen or Prudhomme teaches or suggests such a novel use. Therefore, the present invention is not obvious over Chen and Prudhomme. Withdrawal of the rejection is respectfully requested.

In view of the amendment and the above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. In order to expedite prosecution, the Examiner is invited to contact Applicant's undersigned representative at the number listed below to discuss any concerns the Examiner may have.

Respectfully Submitted,

Dated: February 23, 2005

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